Dr. H. Fraenkel-Conrat,
The Virus Laboratory,
University of California,
BERKELEY 4,
California, U.S.A.

21st February, 1956.

Dear Dr. Fraenkel-Conrat,

I enclose two short manuscripts by Don Caspar and myself, which we are sending to "Nature". You may also have seen a brief summary which I recently sent to Professor Stanley, describing the same results.

As you will see, it is your Hg-TMV which has made it possible to determine the location of the RNA in TMV. I think there can be little doubt that the RNA backbone chain(s?) lie on a radius close to 40 A. It is not yet possible to decide whether there is a single RNA molecule following the line of the main protein helix or 15 molecules running along coaxial helices of angle about 45°. If anything, the X-ray evidence favours the former, though this is obviously an awkward model from other points of view.

In my last letter to you I said that there were 46 protein units in the 69 A period. I am now inclined to think that the number is 49 rather than 46, which makes the molecular weight situation a little easier, though still awkward if the particle weight is as high as 50 million. In any case there is no evidence left for the earlier suggestions of 31 or 37.

The substance which would help more than any other in the next stage of the work - the determination of the chain direction and molecular structure of the RNA - is your mercury-substituted repolymerised protein. Unfortunately I was not successful with what you sent me. I obtained only one specimen which did not depolymerise when orientated and that one was good enough only for qualitative measurements. If you ever have a few more milligrams of this substance to spare I should be extremely grateful for them. If you do send me some, would you please specify exactly what buffer solution should be used with it, as I think it might be best for me

to re-suspend it and try to orientate it immediately after centrifuging. Alternatively, would it be better for you to send it in the form of a solution, for me to centrifuge? (Originally I asked you to send everything in the form of pellets because I had no centrifuge available, but I have recently acquired a centrifuge).

Having determined the radius on which the Hg lies, and the magnitude of its contribution to the equator in Hg-TMV, I can now use the comparison of TMV and Hg-TMV to give the phase of the intensity maxima on the layer-lines of TMV. If I were able to do the same thing for the repolymerised protein by comparing it with Hg-protein I should be in a position, in theory at least, to determine the phase and magnitude of the RNA contribution on the layer-lines from a comparison of the TMV and protein data, and hence to calculate a Fourier for the RNA. All this would be a long job, but, I think, well worth while.

Best wishes,

Yours sincerely,

Rosalind Franklin.